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PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE, SUITE 1200
1201 PEACHTREE STREET
ATLANTA, GA 30361

| EXAMINER | |
|---|---|
| MCELWAIN, ELIZABETH F | |
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**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Application Number: 09/991,152
Filing Date: November 16, 2001
Appellant(s): AQUIN ET AL.

Patrea L. Pabst
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed December 28, 2006 appealing from the Office action mailed August 28, 2006 and the Information Disclosure Statement filed September 6, 2007.

**(1) Real Party in Interest**

A statement identifying by name the real party in interest is contained in the brief.

**(2) Related Appeals and Interferences**

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**(3) Status of Claims**

The statement of the status of claims contained in the brief is correct.

**(4) Status of Amendments After Final**

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

**(5) Summary of Claimed Subject Matter**

The summary of claimed subject matter contained in the brief is correct.

**(6) Grounds of Rejection to be Reviewed on Appeal**

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

**NEW GROUND(S) OF REJECTION**

Claim 6 is objected to for being a duplicate to claim 5 in that the wording is identical and both depend from claim 1.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 3-9, 11 and 13-26 are rejected under 35 U.S.C. 102(a) as being anticipated by Poirier et al (Plant Physiology 121:1359-1366, 1999).

The claims are drawn to bacteria or plants that produce PHA and that comprise a transgene encoding 3-hydroxyl-ACP thioesterase and an acyl-CoA synthetase for the production of medium chain length PHA. It is noted that Appellant uses PHA synthase interchangeably with PHA synthetase in the Brief.

Poirier et al teach Arabidopsis plants coexpressing transgenes encoding a medium chain length acyl- ACP thioesterase and an acyl-CoA synthase for the production of medium chain length PHA, wherein PHA is synthesized from the polymerization of the 3-hydroxyacyl-CoA intermediates (see the abstract; page 1360, the first full paragraph and the second column, including Figure 1, for example). Poirier et al also teach a modified enzyme (at page 1360,

second column, the first sentence of the first full paragraph) and use of a napin promoter for targeting expression in the seed (see Figure 1). In addition, Poirier et al teach use of kanamycin for selection of transformants, indicating that selectable marker genes were also expressed.

Claims 1, 3-13, 15-20, 22-26, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Poirier et al (Plant Physiology 121:1359-1366, 1999) taken with Kruger et al (U.S. Patent 5,750,848).

The claims are drawn to bacteria or plants that produce PHA and that comprise a transgene encoding 3-hydroxyl-ACP thioesterase for the production of medium chain length PHA.

Poirier et al teach Arabidopsis plants coexpressing transgenes encoding a medium chain length acyl- ACP thioesterase and an acyl-CoA synthase for the production of medium chain length PHA, wherein PHA is synthesized from the polymerization of the 3-hydroxyacyl-CoA intermediates (see the abstract; page 1360, the first full paragraph and the second column, including Figure 1, for example). Poirier et al also teach a modified enzyme (at page 1360, second column, the first sentence of the first full paragraph) and use of a napin promoter for targeting expression in the seed (see Figure 1). In addition, Poirier et al teach use of kanamycin for selection of transformants, indicating that selectable marker genes were also expressed.

Poirier et al do not teach a method of producing PHA in bacteria.

Kruger et al teach the production of PHAs in bacteria and plants (abstract, sentence bridging columns 2-3 and Figure 1). Kruger et al also teach that medium chain length monomers may be made in bacteria (columns 1-2).

Given the recognition of Poirier et al of the use of transgenes encoding a medium chain length acyl- ACP thioesterase and an acyl-CoA synthase for the production of medium chain length PHA in a plant and the teaching of Kruger et al of the production of medium chain length PHA in bacteria, it would have been obvious to use the transgenes taught by Poirier et al to transform bacteria for the production of medium chain length PHA. Thus the claimed invention would have been prima facie obvious as a whole at the time it was made, especially in the absence of unexpected results.

**(7) Claims Appendix**

The copy of the appealed claims contained in the Appendix to the brief is correct.

**(8) Evidence Relied Upon**

| | | |
|---|---|---|
| 5,750,848 | KRUGER | 5-1998 |

Poirier et al, Plant Physiology 121:1359-1366, December 1999

**(9) Grounds of Rejection**

The following ground(s) of rejection are applicable to the appealed claims:

***Claim Rejections - 35 USC § 103***

Claims 1, 3-13, 15-20, 22-26, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kruger et al (U.S. Patent 5,750,848).

The claims are drawn to bacteria or plants that produce PHA and that comprise a transgene encoding 3-hydroxyl-ACP thioesterase for the production of medium chain length PHA. Appellants assert that 3-hydroxyl-ACP thioesterase is taught by Kruger et al and disclosed as *PhaG*.

Kruger et al teach *PhaG* for the production of PHAs in bacteria and plants (abstract, sentence bridging colums 2-3 and Figure 1). Kruger et al teach that *PhaG* can be used in conjunction with other PHA biosynthetic genes, including PHA synthase (which Appellant uses interchangeably with PHA synthetase in the Brief), to produce novel, biodegradable polyesters. Kruger et al also teach that "any enzyme or combination of enzymes that convert beta-hydroxyacyl-ACP to beta-hydroxyacyl-CoA could be cloned by transforming a PHA negative bacterium harboring only a PHA synthase (column 14, lines 3-14). Kruger et al teach the *PhaG* transformed into E. coli as fragment E3 enabled mutant cells to accumulate PHA. Kruger et al also teach that medium chain length monomers may be made in plants (column 26, lines 46-59) and bacteria (columns 1-2), and methods of transforming plants and bacteria, including expression of a marker gene (column 24, line52) and targeted expression to a specific tissue or organelle, such as to seeds or plastids, for example (column 25, lines 16-25).

Kruger et al do not specifically teach medium chain PHA produced in bacteria and plants transformed with a gene encoding 3-hydroxyl-ACP thioesterase or plants transformed with said gene.

Given the recognition of those of ordinary skill in the art of the value of producing novel biodegradable polyesters, as taught by Kruger et al, it would have been obvious to use the teachings of Kruger et al to use the *PhaG* gene encoding 3-hydroxyl-ACP thioesterase in

combination with other PHA biosynthetic genes, such as PHA synthase, to transform bacteria or plants using the methods described by Kruger et al to produce novel biodegradable polyesters, such as medium chain PHA and it would have been obvious to include a marker gene in the transformation construct and to use known plant promoters for tissue specific or plastid expression. Thus the claimed invention would have been prima facie obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

**(10) Response to Argument**

Appellants argue that they "have discovered a novel way to produce medium chain length PHAs in organisms that do not naturally produce them, via the fatty acid biosynthetic route, using an acyl-ACP-CoA transferase, encoded by the phaG gene" (page 4 of the Brief filed December 28, 2006). However, the Examiner maintains that Appellants' specification teaches that use of the phaG gene for producing PHA biopolymers was known in the prior art (see page 3, lines 5-19 of the specification). Appellants assert that transformation of *E. coli* with coding sequences for acyl-CoA transferase and PHA synthetase in the prior art were unsuccessful in producing medium chain length PHAs because the conditions used in the prior art caused the acyl-CoA transferase to function as a thioesterase. Appellants state that the 3-hydroxy fatty acid substrates required by the PHA synthase would not be produced by thioesterase activity and assert that they have shown production of medium chain length PHAs by expressing 3-hydroxyacyl-ACP thioesterase (phaG) and other genes having either acyl-CoA synthetase activity or acyl CoA transferase activity. The Examiner maintains that Appellant is arguing

limitations that are not in the claims with regard to different culture conditions that may be required. Claims 1-12 and 29 are drawn to organisms and not to conditions for culturing said organisms, and claims 13, 15-26 and 30 are drawn to methods, but the claimed methods do not include limitations with regard to conditions for culturing the bacteria or plants for production of medium chain length PHAs.

In addition, Appellants state that the prior art did not teach the need to provide acyl-ACP-CoA transferase in combination with an acyl-CoA synthetase or acyl-CoA transferase in order to produce PHAs. The Examiner maintains that again Appellants are arguing limitations that are not in the claims, given that the claims are not drawn to the requirement of having acyl-ACP-CoA **transferase** in combination with an acyl-CoA synthetase or acyl-CoA transferase. The claims are drawn to organisms and methods requiring a transgene encoding **3-hydroxyacyl-ACP thioesterase** and other genes having **either** acyl-CoA synthetase activity **or** acyl CoA transferase activity.

Appellants argue that the rejection does not meet the requirements for establishing a rejection under 35 U.S.C. 103 given that the claims require at least two transgenes and that at least one additional transgene would have acyl-CoA synthetase or acyl-CoA transferase activity so that medium chain length PHA accumulates. Appellants assert that Kruger's work relied on an endogenous enzyme and not a transgene. Appellant argues that Kruger discloses two transgenes: the phaG gene and a gene encoding PHA synthetase, but then Appellant argues that "one must have three genes" (at page 7, line 13 of the Brief). The Examiner maintains that again Appellant is arguing limitations that are not in the claims. The claims do not require a PHA

synthetase in addition to a transgene encoding 3-hydroxyacyl-ACP thioesterase and a transgene having either acyl-CoA synthetase activity or acyl CoA transferase activity.

Furthermore, Appellants state that Kruger does not teach transforming an organism with two transgenes, and that Kruger does not provide evidence that 3-hydroxyacyl-ACP thioesterase activity is present in phaG, suggesting that the thioesterase activity may be provided by another endogenous enzyme. The Examiner maintains that Appellants have asserted that phaG provides thioesterase activity, and that Kruger at column 3, line 46 and in Figure 1 relates thioesterase activity to phaG. In addition, the difference between a gene being a transgene or an endogenous gene would not patentably distinguish the claimed invention. The existence of the required enzymes would make obvious the claimed organisms and methods.

Appellant goes on to suggest that the skilled artisan would understand that a protein having two different enzyme activities would require different conditions for each activity. The Examiner maintains that again Appellant is arguing limitations that are not in the claims, given that the claims do not recite any conditions required for phaG to function as a thioesterase.

Appellant argues that Kruger does not refer to either acyl-CoA synthetase or acyl CoA transferase as PHA biosynthetic genes, and that Kruger does not disclose dual enzyme activity of the enzyme encoded by phaG. However, the Examiner maintains that Kruger discloses the requirement for enzymes having acyltransferase activity and that there may be both acyltransferase activity and thioesterase activity associated with phaG (see Figure 1, at least). Also, the Examiner maintains that Appellant hasn't provided a definition of PHA biosynthetic enzymes in the specification that would exclude those taught by Kruger.

In addition, Appellant has argued (at page 9, the first paragraph of the Brief, for example) that phaG is an acyl-CoA transferase as well as a thioesterase. Appellant further asserts that acyl-ACP-CoA transferase activity has been previously demonstrated, as taught in the specification at pages 2-3, so that the skilled artisan would not have been motivated to engineer an organism with a transgene encoding that activity. The Examiner maintains that the claims do not require that the organism be transformed with an acyl-CoA transferase. The claims only require that the organism be transformed with either an acyl-CoA synthetase or an acyl-CoA transferase, along with a 3-hydroxyacyl-ACP thioesterase.

Appellants assert that Kruger does not meet every limitation of the claims given that Kruger does not teach that a gene encoding an acyl-CoA transferase or synthetase is essential to make PHAs. The Examiner maintains that Appellant has stated that phaG also encodes acyl-CoA transferase activity, but does not disclose that phaG encodes 3-hydroxyacyl-ACP thioesterase. The Examiner maintains that the phaG sequence that Appellants use is the same as that taught by Kruger et al, which would inherently have 3-hydroxyacyl-ACP thioesterase activity. In addition, Kruger et al teach that phaG can be used in conjuction with other PHA biosynthetic genes, as stated previously, and the evidence for non-obviousness should be commensurate with the scope of the claims.

Finally, Appellants argue that no art has been cited with regard to targeting PHA production to specific organelles of a plant or expression of marker genes in a plant or that would lead one to know that a 3-hydroxyacyl-ACP thioesterase and PHA synthase could produce PHAs via medium chain substrates. The Examiner maintains that Kruger teaches the requirement for a 3-hydroxyacyl-ACP thioesterase (phaG) and PHA synthase (phaC). The Examiner also

maintains that Appellant has confused the issues by substituting different enzyme names in the arguments. The claims are drawn to use of an acyl-CoA synthetase or an acyl-CoA transferase, but here Appellants have used the name PHA synthase. The Examiner clarifies that claims 11 and 25 are drawn to targeting expression to tissues or organelles that include seeds and leaf, not just to organelles. Kruger teaches at column 24, line 52 the desirability of using a selectable marker in plant transformation constructs, and at column 25, lines 16-23, Kruger teaches promoters for preferential expression in seed plastids and in seeds, for example.

**(11) Related Proceeding(s) Appendix**

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejection should be sustained.

Respectfully submitted,

Elizabeth F. McElwain

Conferees:

Anne Marie Grunberg

TC1600 Director (Acting)

Gary Benzion

GARY BENZION, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600